Remarks

Introduction

Claims 19, 20, and 22-24 were pending. By way of this response, the specification and claim 19 have been amended and claim 25 has been added. Support for the amendments to the specification and the claims can be found in the application as originally filed, and care has been taken to avoid adding new matter. Accordingly, claims 19, 20, and 22-25 are currently pending.

The specification has been amended as set forth above to address any potential confusion resulting from the preliminary amendment filed with the original specification of the above-identified application on July 28, 2003.

In that regard, the preliminary amendment filed on July 28, 2003 presented amendments to the specification which included six paragraphs (not including the section headings and title). The amendments of the specification included an amendment of the title and the addition of the cross-reference to related applications.

Importantly, **as of the filing date** of the above-identified application, the above-identified application claimed priority under 35 U.S.C. § 120 to, and incorporated by reference both, U.S. application number 10/114,740 and U.S. application number 09/371,354 (see page 6 of the preliminary amendment filed on July 28, 2003). Therefore, applicant submits that the above-identified application, **as of its filing date**, properly claimed priority to and incorporated by reference, U.S. application

number 10/114,740, which was filed on April 1, 2002, and U.S. application number 09/371,354, which was filed on August 10, 1999. In view of the above, applicant submits that the above-identified application **has a priority date of August 10, 1999** with respect to subject matter that was originally disclosed in U.S. Application No. 09/371,354 and includes such subject matter as part of the above-identified application as filed.

The other paragraphs presented in the preliminary amendment, which paragraphs were not amended, correspond to the first few paragraphs of U.S. application number 09/371,354 (i.e., the grandparent of the above-identified application). Apparently, this presentation has confused the Examiner causing the Examiner to believe that the above-identified application is not actually a continuation application of U.S. application number 10/114,740 (i.e., the parent of the above-identified application).

In attempt to mitigate this confusion, by way of this Amendment, applicant has amended the specification. In particular, applicant has essentially replaced the three unamended paragraphs that were presented in the preliminary amendment and that corresponded to the first three paragraphs of the grandparent application, with the first three paragraphs of the specification of the above-identified application, as originally filed. In addition, the specification includes the title and the cross-reference to related applications section as presented in the July 28, 2003 preliminary amendment. Applicant has reviewed the specification of the above-identified application as originally filed against the specification of the parent application (U.S. application number 10/114,740) and

confirms that the specifications are identical. Thus, applicant submits that the record clearly shows that the present application (U.S. Application No. 10/628,905) is a continuation application of U.S. Application No. 10/114,740, and U.S. Application No. 10/114,740 is a continuation-in-part of U.S. Application No. 09/371,354.

In addition, and in response to the Examiner's comments regarding the July 28, 2003 preliminary amendment amending pages 6 and 7 of the specification of the above-identified application, applicant submits that the numbering identified by the Examiner corresponded to the page numbers of the July 28, 2003 preliminary amendment. In particular, "pages 6 and 7" which included the amendments to the specification were the page numbers of the preliminary amendment, and not the pages of the specification. In the July 28, 2003 preliminary amendment, the first page clearly states that the preliminary amendment "amends **page 1** of the specification" (emphasis added) and the top of page 6 of the preliminary amendment states that "the following is a marked up version of **page 1** of the specification" (emphasis added). Thus, applicant submits that it was clear that the amendments to the specification presented in the July 28, 2003 preliminary amendment were directed only to the first page of the specification of the above-identified application, and not to pages 6 and 7 of the specification, as proposed by the Examiner.

In addition, the specification has been amended as set forth above by adding a page number at the bottom center of page 1.

In summary, applicant submits that the amendments to the specification as set forth above resolve any confusion presented by the July 28, 2003 preliminary amendment, and clearly establish that the above-identified application, as of its filing date, is a continuation application of U.S. application number 10/114,740, which is a continuation-in-part of U.S. application number 09/371,354. Thus, the priority date of the above-identified application is August 10, 1999.

Objections

The specification has been objected to for not having page numbers.

As indicated in the response filed July 13, 2004, the pages of the specification did in fact include page numbers at the center of the bottom of each page, beginning at page 2. A copy of page 2 as filed is enclosed herewith as **Exhibit A**.

In addition, pursuant to 37 CFR § 1.52(b)(5), applicant encloses herewith a replacement page of the specification which includes the page number --1-- at the bottom center of the page.

In view of the above, applicant submits that the specification is in proper form and requests that this objection regarding page numbers be withdrawn.

Objection/Rejection to the Specification

The specification has been objected to for failing to provide proper antecedent basis for the phrase "wherein the

botulinum toxin elutes from the stent". The amendment filed on July 28, 2003 has been objected to for introducing new matter. In particular, the Office Action states that the oath/declaration, transmittal letter, and original specification introduce new matter because they conflict with regard to the particular relationships of the parent application. More specifically, the Office Action states that the July 28, 2003 preliminary amendment identifies that the above-identified application is a continuation application of U.S. Application No. 10/114,740, but that the transmittal cover letter states that the application is a continuation-in-part of U.S. Application No. 10/114,740. In addition, the Office Action points to discrepancies between pages 6 and 7 of the preliminary amendment and pages 6 and 7 of the specification. In addition, the Office Action states that the "incorporation by reference" is new matter since it was added after the filing date of the application.

Regarding the new matter issues discussed above, applicant traverses the objections/rejections.

First, applicant submits that the transmittal letter **does not** indicate that the above-identified application is a continuation-in-part of U.S. Application No. 10/114,740. A copy of the transmittal letter is submitted herewith as **Exhibit B**. The transmittal letter specifically states that the above-identified application "claims priority to both of: continuation in part application Serial Number 10/114,740, filed April 1, 2002, which is a continuation in part of pending application Serial Number 09/371,354, filed August 10, 1999." Clearly, the initial phrase "continuation in part" is referring to the

application Serial Number 10/114,740. In short, the transmittal letter has identified U.S. Application No. 10/114,740 as a "continuation in part" two times. It is clear that the statement in the transmittal letter does not indicate that the above-identified application is a continuation in part of U.S. Application No. 10/114,740. This is supported by the fact that the actual specification of the above-identified application as filed is identical to the specification of U.S. Application No. 10/114,740.

In addition, as discussed in the Introduction above, pages 6 and 7 referred to the pages of the preliminary amendment and not the specification. As clearly indicated in the July 28, 2003 preliminary amendment, the amendments to the specification were made to **page 1** of the specification. However, due to the inadvertent use of page 1 from the grand-parent application to the above-identified application, there was some confusion. Applicant submits that the amendments to the specification presented herein resolve any apparent confusion regarding the previous amendments to the specification. For example, the specification as presently amended is identical to the specification as originally filed, except with the addition of a new title, additional inventor, and the Cross-Reference to Related Applications section.

Regarding the incorporation by reference, applicant submits that the subject matter of both U.S. Application No. 10/114,740 and U.S. Application No. 09/371,354 were incorporated by reference **at the time of filing** the above-identified application. In particular, the above-identified application was filed on July 28, 2003. With the filing of the above-

identified application, that is on July 28, 2003, a preliminary amendment was filed, as discussed above. The preliminary amendment included an amendment to the specification that incorporated U.S. Application No. 10/114,740 and U.S. Application No. 09/371,354 by reference. Therefore, the subject matter that was incorporated by reference (i.e., the subject matter of U.S. Application Nos. 10/114,740, and 09/371,354) does not constitute new matter for the above-identified application. Since the incorporation by reference was made on July 28, 2003, i.e., at the time of filing of the above-identified application, applicant submits that the OG Notice cited by the Examiner is nor relevant.

Therefore, in view of the above, applicant submits that the specification does not include new matter with respect to priority claim of the above-identified application or to the incorporation by reference of the parent applications.

Regarding the alleged lack of antecedent basis for the phrase "wherein the botulinum toxin elutes from the stent", applicant submits that support for that phrase is provided on page 26 of U.S. Application No. 09/371,354, which was filed on August 10, 1999, and which was properly incorporated by reference in the above-identified application by way of the amendments to the specification in the Preliminary Amendment filed on July 28, 2003, as discussed above. Therefore, applicant submits that the above-identified application provides proper antecedent basis for the phrase "wherein the botulinum toxin elutes from the stent."

In view of the above, applicant submits that the specification of the above-identified application provides proper antecedent basis for the claimed subject matter, and that the specification does not include new matter. Therefore, applicant requests that the objections/rejections of the specification be withdrawn.

Rejection Under 35 U.S.C. § 101

Claim 23 has been rejected under 35 U.S.C. § 101 as claiming the same invention as that of claim 13 and 14 of U.S. Patent No. 6,767,544 (the '544 patent).

Applicant traverses the rejection.

It has been established that the phrase "same invention" with respect to 35 U.S.C. § 101 and double patenting rejections refers to identical subject matter (*In re Vogel*, 422 F.2d 438, 164 USPQ 619 (C.C.P.A. 1970), and see MPEP § 804). To establish a double patenting rejection under 35 U.S.C. § 101, the Office must show that the claims in the issued patent and the pending application cannot be literally infringed without literally infringing one another.

Applicant submits that a *prima facie* case of same-invention double patenting has not been established since the Office Action lacks the necessary literal infringement analysis. Therefore, applicant requests that the rejection be withdrawn.

Nevertheless, applicant submits that the present claims are not for the "same invention" as claims 13 and 14 of the '544

patent. For example, applicant submits that it is possible to literally infringe one or more of the present claims without literally infringing the claim 13 or 14 of the '544 patent.

For example, claim 13 of the '544 patent is as follows:

A composition for use in a coronary arterial cardiovascular procedure comprising a stent for reducing a coronary arterial blockage with a botulinum neurotoxin attached to or imbedded in the stent.

Claim 23 of the above-identified application does not recite that the stent is a component of a composition. Therefore, it is possible to literally infringe claim 23 of the above-identified application without literally infringing claim 13 of the '544 patent.

In view of the above, applicant submits that the present claims satisfy the requirements of 35 U.S.C. § 101, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Obviousness-Type Double Patenting

Claims 19, 20, 22, and 23 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13 and 14 of the '544 patent (identified above) in view of U.S. Patent No. 6,383,509.

Applicant does not concede with the rejection, and reserves the right to traverse the rejections in the future. However, to

advance the prosecution of the above-identified patent application, applicant submits herewith a Terminal Disclaimer over the '544 patent.

In view of the above, applicant submits that the obviousness-type double patenting rejection has been overcome, and applicant requests the rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 19, 20, and 22 have been rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement. In particular, the Office Action states that the specification fails to describe any matrix or material or function of eluting from a stent. The Office Action indicates that the above-identified application cannot rely upon a parent application for subject matter not disclosed in the specification of the above-identified application because the incorporation by reference to U.S. Application No. 09/371,354 by way of the July 28, 2003 Preliminary Amendment was allegedly improper and introduced new matter.

Applicant traverses the rejection.

As discussed above, the subject matter of U.S. Application No. 09/371,354 was incorporated by reference into the specification of the above-identified application on July 28, 2003 (i.e., **at the time of filing** the above-identified application). Therefore, the incorporation by reference of the subject matter of U.S. Application No. 09/371,354 was proper, and the priority date for the present claims is August 10, 1999.

In view of the above, applicant submits that the subject matter of the present claims, and claims 19, 20, and 22 in particular, satisfy the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejection Under 35 U.S.C. § 102

Claims 19, 20, and 22 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Donovan et al. (U.S. Patent No. 6,383,509; the '509 patent). Claims 23 and 24 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Murkerjee et al. (2000), and under 35 U.S.C. § 102(e) as being anticipated by Unger (U.S. Patent No. 6,579,847).

Applicant traverses each of the rejections.

As discussed above, the present application has a priority date of August 10, 1999. The '509 patent was issued on May 7, 2002, and has an effective filing date of June 2, 2000 (i.e., the filing date of U.S. Application No. 09/587,250). Since the present application has a priority date that predates the '509 patent, the '509 patent is not prior art to the present application. Similarly, Murkerjee et al., and Unger are not prior art to the above-identified application since Murkerjee et al. was published and Unger was filed after the priority date of the above-identified application (i.e., after August 10, 1999). Therefore, applicant submits that none of the '509 patent,

Murkerjee et al, and Unger are prior art to the present application.

In view of the above, applicant submits that the present claims, that is claims 19, 20, 22-25, are not anticipated by the '509 patent, Murkerjee et al., or Unger under 35 U.S.C. § 102.

Rejections Under 35 U.S.C. § 103

Claims 19, 20, 22, 23, and 24 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Vigil et al. (U.S. Patent No. 6,102,904) in view of Schramm et al. (U.S. Patent No. 6,121,296) and Rappuoli et al., (1997). In particular, the Office Action states that it would be obvious to a person of ordinary skill in the art to modify the composition of Vigil et al. to substitute the botulinum toxin of Rappuoli et al. for the toxin disclosed by Vigil since Schramm et al. teach both pseudomonas toxin and botulinum toxin function as ADP-ribosylating toxins, and that substitution of one function equivalent for another is routine in the art.

Applicant traverses the rejections.

Vigil et al. discloses a device for injecting fluid into a blood vessel wall. Vigil discloses that either the fluid can contain anti-proliferative agents or the fluid can contain agents which stimulate production of collateral vessels (column 3, lines 37-55). More specifically, Vigil et al. discloses that the anti-proliferative agents are agents that kill rapidly dividing cells (column 3, lines 40-41). In other words, the antiproliferative agents are cytotoxic to cells. Vigil et al.

identifies several cytotoxic agents, among which, pseudomonas exotoxin and ricin A toxin are identified (column 3, lines 45-46). Vigil does not disclose, teach, or even suggest the use of any toxins that are not cytotoxic, let alone any toxins produced from Clostridial bacteria, such as botulinum toxin.

Schramm et al. discloses compounds that inhibit nucleoside hydrolase and transferase enzyme activity of parasites. Schramm et al. attempts to solve the problem of developing a method of preventing purine and pyrimidine salvage by parasitic organisms (column 2, lines 19-21). Schramm indicates that several different bacterial toxins may disrupt cellular function by using NAD+ and transferring ADP-ribose to regulate guanine nucleotide binding proteins when an individual is infected by bacteria which produce such toxins (column 2, lines 3-10). In short, Schramm et al. discloses chemical compounds which may be effective in interfering with the cellular disruption caused by bacterial infection. Schramm et al. does not disclose, teach, or even suggest therapeutic use of any toxin, let alone such use of a Clostridial neurotoxin, such as a botulinum toxin.

Rappuoli et al. discloses general information regarding C2 toxin. Rappuoli et al. discloses that Clostridium botulinum C2 toxin is a member of a family of binary cytotoxins. Significantly, Rappuoli et al. specifically states that "C2 toxin is not a clostridial neurotoxin and plays no role in botulism." (page 67, right column, second paragraph; emphasis added). Rappuoli et al. further states that the Clostridium botulinum C2 toxin and the botulinum C3 ADP-ribosyltransferase are not neurotoxigenic (page 108, left column, first full

paragraph). Thus, Rappuoli et al. specifically states that C2 toxins are not clostridial neurotoxins.

Applicant submits that the combination of Vigil et al., Schramm et al., and Rappuoli et al. do not disclose, teach, or suggest the present invention. For example, the combination of Vigil et al., Schramm et al., and Rappuoli et al. do not disclose, teach, or even suggest a stent, or a composition comprising a stent, or an angioplasty balloon, with a botulinum toxin attached or embedded in the stent or balloon, as recited in the present claims.

As disclosed in the above-identified application, a botulinum toxin, such as the botulinum toxin recited in the present claims, is a type of Clostridial neurotoxin (see page 15 of the specification of the above-identified application). As acknowledged in the Office Action, Vigil et al. does not teach the limitation of a botulinum toxin (see page 14, last sentence of first paragraph). Similarly, as specifically stated in Rappuoli et al., C2 toxins are not clostridial neurotoxins. Therefore, C2 toxins, as disclosed by Rappuoli, are different and distinct from botulinum toxins one from the other. Thus, Rappuoli fails to make up for the deficiencies of Vigil et al. In addition, Schramm et al. does not disclose any botulinum toxin as a component of a stent or angioplasty balloon, let alone, any therapeutic use of a botulinum toxin. In contrast, Schramm et al. discloses compounds which are intended to interfere with bacterial poisoning, which may include botulism.

Thus, applicant submits that the combination of references, including Vigil et al., Schramm et al., and Rappuoli et al.,

fails to disclose, teach, or even suggest all of the elements of the present claims.

In addition, applicant submits that a person of ordinary skill in the art would not be motivated to modify the teachings of Vigil et al. based on the teachings of Schramm et al. and/or Rappuoli et al. For example, the only disclosure by Vigil et al. with respect to toxins is directed to the use of cytotoxic agents to reduce cell proliferation, as discussed above. Schramm et al. is directed to an entirely different problem, that is, the problem of designing chemical compounds to interfere with cell dysfunction caused by bacterial toxins. Rappuoli et al. discloses that C2 toxins are not Clostridial neurotoxins. Thus, since Schramm et al. and Rappuoli et al. disclose agents that are completely structurally and functionally different than the cytotoxic agents disclosed by Vigil et al., applicant submits that a person of ordinary skill in the art would not be motivated to modify the teachings of Vigil et al. based on the teachings of Schramm et al. and/or Rappuoli et al.

Furthermore, even if the references could be erroneously combined, the combination fails to disclose, teach, or even suggest all of the elements recited in the present claims.

In view of the above, applicant submits that the present claims, that is claims 19, 20, and 22-25, are unobvious from and patentable over Vigil et al., Schramm et al., and Rappuoli et al., taken alone or in any combination, under 35 U.S.C. § 103.

Conclusion

In conclusion, applicant has shown that the present specification is in proper form, that the present claims are not subject to double patenting, satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 19, 20, and 22-25, are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Date: 2/17/05

Respectfully submitted,

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Stents are often used in combination with coronary balloon angioplasty. Typically, a stent is used to brace the blood vessel open after an initial expansion of the narrowed blood vessel by a balloon. Self expanding stents are also used to expand and hold open occluded blood vessels. Various stents and their use are disclosed in U.S. Patent Nos. 6,190,404; 6,344,055; 6,306,162; 6,293,959; 6,270,521; 6,264,671; 6,261,318; 6,241,758; 6,217,608; 6,196,230; 6,183,506; 5,989,280. The disclosure of each of these patents is incorporated in its entirety herein by reference.

One problem with angioplasty is that following the procedure restenosis, or recurrence of the obstruction, may occur. Tears in the wall expose blood to foreign material and proteins, such as collagen, which are highly thrombogenic. Resulting clots can contain growth hormones which may be released by platelets within the clot. Additionally, thrombosis may cause release of growth hormones and cytokines by cells from macrophages. Growth hormones may cause smooth muscle cells and fibroblasts to aggregate in the region and multiply. Further, following angioplasty there is often a loss of the single layer of cells that normally covers the internal surface of blood vessels which leads to thrombosis. The combination of tearing of the blood vessel wall and the loss of the endothelial layer often generates an internal blood vessel surface which is quite thrombogenic. Restenosis may result from the proliferation of smooth muscle cells, which normally reside within the arterial wall, in the area of the injury in response to the thrombosis.

Angioplasty procedures also produce injuries in the arterial wall which become associated with inflammation. Any kind of inflammatory response may cause growth of new tissue, for example, scar tissue, which may contribute to restenosis.